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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/049,696	03/27/98	BILLING-MEDEL	P 6067.US.01

EXAMINER	
KERR, I	
ART UNIT	**PAPER NUMBER**
1633	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/049,696	Applicant(s) BILLING-MEDEL ET AL.	
	Examiner Janet Kerr	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *7-10,12-14 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,11,15,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Response to Amendment

Applicants' amendment and the declaration of Paula N. Friedman, filed 11/16/00, have been entered.

Claims 1-18 remain pending.

Claims 7-10, 12-14, and 16 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

Claims 1-6, 8, 11, and 15 are being examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 15, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Newly amended claims 1, 5, 15, 17, and 18 recite the limitation of "polynucleotides having at least 95% identity". However, the specification does not disclose polynucleotides having at least 95%, nor is there recitation of polynucleotides having at least 95% identity in the claims as originally filed. Applicants are required to cancel the claims or amend the claims such that the claimed invention is supported by the disclosure in the instant application.

This is a new matter rejection.

Claims 1-6, 11, 15, 17, and 18 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons of record and the reasons below.

As stated in the previous office action, the specification discloses that the polynucleotides of the instant invention are partially homologous to a polynucleotide encoding a bovine chloride channel protein (see page 53, lines 11-14 of the instant application). However, the specification does not indicate the degree of homology to the bovine chloride channel, either with respect to the polynucleotide or polypeptide, or the structural features which render the polypeptide structurally similar to the bovine chloride channel protein. In addition, the specification does not provide polynucleotide or polypeptide sequence comparisons, nor does the specification identify any common structural motifs associated with the disclosed peptides and which are contained in putative the putative chloride channel polypeptide. Moreover, no biological activities have been established for the polypeptides encoded by the polynucleotide. Thus, with regard to the asserted utilities disclosed in the application, inasmuch as the function of the polypeptide is not known, further research would be required to assess the biological relevance of the expression of CS194 in tissues.

Claims 1-6, 11, 15, 17, and 18 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for the reasons of record. Moreover, with respect to the newly added limitation of polynucleotides having at least 95% identity, the specification does not disclose such polynucleotides, nor does the specification provide guidance as to which nucleotides should be altered to make the nucleotides. There is no teaching in the specification of whether the alterations are over the entire length of the polynucleotide, or are limited to a particular location of the polynucleotide. Thus, one of skill in the art would not

know, *a priori*, how to make the polynucleotides as claimed, nor would the skilled artisan know how to use the claimed polynucleotides.

Applicant's arguments filed 11/16/00 have been fully considered but they are not persuasive. It is initially argued that CS194 is a well known chloride channel. This is not persuasive as the specification only states that CS194 is partially homologous to the bovine chloride channel. There is no indication in the specification that CS194 is a well known chloride channel, and applicants have not provided any objective evidence demonstrating that the claimed polynucleotides encode a functional chloride channel.

It is further argued that the novel chloride channel is specific to the colon and is regulated by guanylyl cyclase C (GCC) or a GCC homologue. Applicants provide a discussion on the function and utility of GCC as a highly tissue specific marker for colorectal cancer. Applicants assert that it is evident that CS194 has a definite link to cancer and makes it an excellent cancer marker when used to detect tumor growth in the digestive tract. These arguments are not persuasive as there is no teaching in the specification of regulation of CS194 by GCC or a homologue thereof, or that CS194 is linked to cancer, and thus makes it an excellent cancer marker when used to detect tumor growth in the digestive tract.

Applicants argue that CS194 has high tissue specificity, that the polynucleotide is useful as a diagnostic marker for diseases of the GI tract due to its abundance in GI tract tissue, and specifically indicate that CS194 is approximately 104 times more abundant in GI tissue than in the rest of the body. Applicants further assert that it is known in the art that a gene product which is more prevalent and highly specific to one tissue type than other tissue types is extremely useful as a marker for the detection of disease in that tissue. Applicants indicate that if a protein appears in a tissue or body compartment where its normal occurrence is very low or non-existent, then the specific tissue in which the protein is normally found is in a diseased state. This is because the disease causes an alteration to the protein-specific tissue resulting in the protein escaping from its normal tissue into another. The examiner does not understand these arguments. Applicants initially argue that CS194 is tissue specific, i.e., is approximately 104

times more abundant in GI tissue than in the rest of the body. Is this abundance naturally occurring or a result of a cancerous condition? Does this protein escape from GI tissue and target to a tissue or body compartment where the expression of the CS194 gene is normally very low or non-existent?

Applicants provide an analogy among the cancer markers PSA and CEA, and CS194. Applicants indicate that PSA is normally found in the prostate, but detection of PSA in the blood is indicative of prostate cancer. Similarly, CEA is normally found in the colon and in stool samples, however, CEA detection in blood at "elevated" levels is indicative of colorectal cancer. Exhibit A is provided which illustrates the usefulness of tissue specific molecules which, upon detection in the circulation, indicate proliferative disease. However, the specification does not provide any objective evidence that a CS194 gene product is detectable in the circulation, nor does the specification provide any nexus between CS194 expression, *per se*, and proliferative diseases of the intestine.

The declaration under 37 CFR 1.132 filed 11/16/00 is insufficient to overcome the rejection of claims 1-6, 11, 15, 17, and 18 based upon 35 USC 101 as set forth in the last Office action because:

The declaration is directed to a comparison of the tissue-specificities of CEA, PSA, and CS194. It is stated that both CEA and PSA are tissue-specific markers that has been shown to be highly expressed in the GI tract and prostate, respectively, and that the PSA gene product is used in screening, prognosis, and monitoring prostate cancer patients (see paragraphs 8 and 9). It is also indicated that to those skilled in the art, PSA and CEA are well known tumor markers, which indicate cancer of the prostate (PSA) or cancer of the GI tract (CEA) when the respective gene product is found in the blood sample of a patient (see paragraph 10). Declarant Friedman asserts that given the similar characteristics of tissue-specificity and abundance of PSA, CEA, and CS194, and in view of the well established utility of detecting PSA and CEA in blood as a diagnostic for cancer, CS194 gene products would also be suitable as cancer diagnostics. As stated previously, this argument is not persuasive as there is no objective evidence in the

specification, in the declaration, or in applicants' Remarks which correlates the expression and/or detection of CS194 gene products in tissues and cancer.

Applicants also argue that the claimed invention has credible utility. The examiner is not arguing a lack of credible utility, rather a specific and substantial utility or a well-recognized utility. Applicants arguments have been directed to the utility of CS194 gene products as diagnostic markers for cancer. Applicants state that "Clearly, the appearance of a secreted CS194 gene product outside the GI tissue itself, such as in whole blood, urine, stool or serum, indicates a form of GI tract disease, akin to the presence of markers such as PSA and CEA found in blood outside of their prevalent tissue type.". This is not persuasive as there is no evidence in the specification that the detection of CS194 gene products outside the GI tissue itself is associated with cancer. Thus, for the reasons of record and the reasons discussed above, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is rendered vague and indefinite because as amended, the claim reads as follows: "which codes for a protein...". It is not clear what codes for a protein, i.e., it is not clear how applicants intended to amend the claim.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to Deborah Clark, Supervisory Primary Examiner of Art Unit 1633, at (703) 305-4051. Any administrative or procedural questions should be directed to Kimberly Davis, Patent Analyst, at (703) 305-3015. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401.

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